

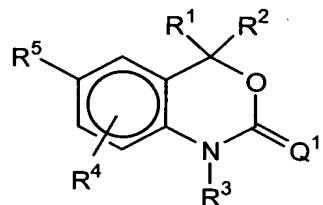
## AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

## Listing of Claims:

1(Currently Amended). A method of inducing contraception comprising the step of delivering to a female of child-bearing age a composition comprising a compound of formula I or formula II, or a tautomer thereof, in a regimen which involves delivering a pharmaceutically effective amount of one or more of a selective estrogen receptor modulator to said female,

wherein formula I is:



I

wherein:

R<sup>1</sup> and R<sup>2</sup> are independent substituents selected from the group consisting of H, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>2</sub> to C<sub>6</sub> alkenyl, C<sub>3</sub> to C<sub>8</sub> cycloalkyl, phenyl, and thiophene;

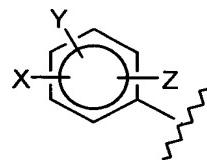
or R<sup>1</sup> and R<sup>2</sup> are fused to form a carbon-based 3 to 8 membered saturated spirocyclic ring;

R<sup>3</sup> is H

R<sup>4</sup> H;

R<sup>5</sup> is selected from the group consisting of (i) and (ii):

(i) a substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN, C<sub>1</sub> to C<sub>3</sub> alkyl, substituted C<sub>1</sub> to C<sub>3</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> alkoxy, NO<sub>2</sub>, and C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl;

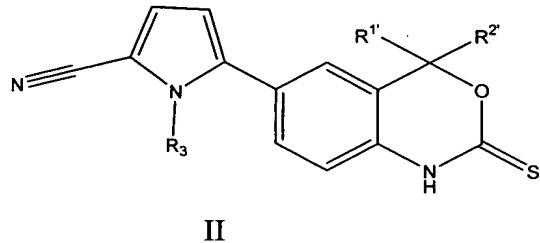
Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO<sub>2</sub>, C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>4</sub> alkyl, and substituted C<sub>1</sub> to C<sub>4</sub> alkyl; and

(ii) a five or six membered carbon-based heterocyclic ring having in its backbone 1 heteroatom selected from the group consisting of O, S, and NR<sup>6</sup> and having one or two independent substituents selected from the group consisting of H, halogen, CN, C<sub>1</sub> to C<sub>4</sub> alkyl, and substituted C<sub>1</sub> to C<sub>4</sub> alkyl;

R<sup>6</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, and C<sub>1</sub> to C<sub>4</sub> CO<sub>2</sub>alkyl;

Q<sup>1</sup> is S;

and formula II is:



wherein:

R<sup>1'</sup> is selected from the group consisting of methyl, ethyl, and trifluoromethyl;

R<sup>2'</sup> is selected from the group consisting of methyl, ethyl, and trifluoromethyl; or

R<sup>1'</sup> and R<sup>2'</sup> are joined to form a spirocyclic ring containing 3 to 7 carbon atoms; and R<sup>3'</sup> is selected from the group consisting of C<sub>1</sub> to C<sub>4</sub> alkyl;

or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug of formula I or formula II.

2(Original). The method according to claim 1, wherein said compound of formula I or formula II and said selective estrogen receptor modulator are delivered in a single composition.

3(Original). The method according to claim 1, wherein said compound of formula I or formula II and said selective estrogen receptor modulator are delivered separately.

4(Original). The method according to claim 1, wherein said selective estrogen receptor modulator is selected from the group consisting of EM-800, EM-652, raloxifene hydrochloride, arzoxifene, lasofoxifene, droloxifene, idoxifene, levormeloxifene, centchroman, nafoxidene, tamoxifen citrate, 4-hydroxytamoxifen citrate, clomiphene citrate, toremifene citrate, pipendoxifene, and bazedoxifene.

5(Original). The method according to claim 1, wherein said compound is delivered at a daily dosage of about 0.1 to about 50 mg.

6(Original). The method according to claim 1, wherein said regimen comprises delivering said composition daily for 1 to about 21 days, wherein said regimen is a cycle which is repeated monthly.

7(Original). The method according to claim 1, wherein said selective estrogen receptor modulator is delivered at a daily dosage of about 0.2 to about 100 mg.

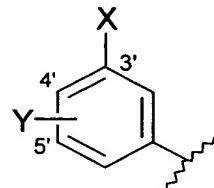
8(Currently Amended). The method according to Claim 1, wherein in formula I:

$R^5$  is the five or six membered ring, wherein said one or two independent substituents are selected from the group consisting of H, halogen, CN, NO<sub>2</sub>, C<sub>1</sub> to C<sub>3</sub> alkyl, and C<sub>1</sub> to C<sub>3</sub> alkoxy.

9(Previously Presented). The method according to claim 8, wherein in formula I:

$R^1$  and  $R^2$  and are independently selected from the group consisting of  $C_1$  to  $C_3$  alkyl and substituted  $C_1$  to  $C_3$  alkyl;

$R^5$  is the substituted benzene ring having the structure:

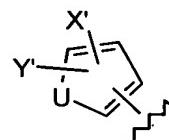


$X$  is selected from the group consisting of halogen, CN,  $C_1$  to  $C_3$  alkoxy,  $C_1$  to  $C_3$  alkyl,  $NO_2$ , and  $C_1$  to  $C_3$  perfluoroalkyl.

10(Previously Presented). The method according to Claim 8, wherein in formula I:

$R^1$  and  $R^2$  and are independently selected from the group consisting of  $C_1$  to  $C_3$  alkyl and substituted  $C_1$  to  $C_3$  alkyl;

$R^5$  is the five membered ring having the structure:



$U$  is selected from the group consisting of O, S, and  $NR^6$ ;

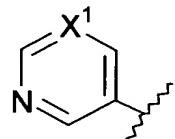
$X'$  is selected from the group consisting of halogen, CN, and  $C_1$  to  $C_3$  alkyl;

$Y'$  is selected from the group consisting of H, halogen, CN, and  $C_1$  to  $C_4$  alkyl.

11(Previously Presented). The method according to claim 8, wherein in formula I:

$R^1$  and  $R^2$  and are independently selected from the group consisting of  $C_1$  to  $C_3$  alkyl and substituted  $C_1$  to  $C_3$  alkyl;

$R^5$  is the six membered ring having the structure:



$X^1$  is selected from the group consisting of N and CX<sup>2</sup>;

$X^2$  is selected from the group consisting of halogen and CN.

12-13(Canceled).

14(Original). The method according to claim 1, wherein in formula I:  $R^1$  and  $R^2$  are fused to form a carbon-based 3 to 6 membered saturated spirocyclic ring.

15-24(Canceled).

25(Original). The method according to claim 1 wherein said compound of formula I is selected from the group consisting of 6-(3-Chlorophenyl)-4,4-dimethyl-1,4-dihydro-benzo[d][1,3]oxazin-2-thione, 4-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-thiophene-2-carbonitrile, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-5-fluorobenzonitrile, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-benzonitrile, 6-(3-fluorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-methylthiophene-2-carbonitrile, tert-Butyl 2-cyano-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-1-carboxylate, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-2-carbonitrile, [6-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-pyridin-2-yl]acetonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1H-pyrrole-2-carbothiamide, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-thiophene-3-carbonitrile, 5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-

1-ethyl-1H-pyrrole-2-carbonitrile, 4-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazin-4,1-cyclohexan]-6-yl)-2-thiophenecarbonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-fluorobenzonitrile, 6-(5-Bromopyridin-3-yl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chloro-5-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-methylphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-trifluoromethoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazin-4,1-cyclohexan]-6-yl)-5-fluorobenzonitrile, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-methylbenzonitrile, 6-(3,5-Dichlorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-1,2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)isophthalonitrile, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-furonitrile, 4,4-Diethyl-6-(3-nitrophenyl)-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chlorophenyl)-4-methyl-4-phenyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 4-Allyl-6-(3-chlorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-Chloro-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)benzonitrile, 6-(3,5-Difluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Fluoro-5-methoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-methoxybenzonitrile, 6-(3-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-[3-Fluoro-5-(trifluoromethyl)phenyl]-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(2-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3,4-Difluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(4-Fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-fluorobenzonitrile, 6-(2,3-Difluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 3-(8-Bromo-4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-5-fluorobenzonitrile, 4,4-Dimethyl-6-(3-nitrophenyl)-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Chlorophenyl)-4,4-diethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Methoxyphenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-

benzoxazine-2-thione, 6-(2-Chlorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 4-Benzyl-6-(3-chlorophenyl)-4-methyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 6-(3-Bromo-5-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)thiophene-2-carbonitrile, 3-Fluoro-5-(8-fluoro-4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)benzonitrile, 3-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)benzonitrile, 5-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)-4-methyl-2-thiophenecarbonitrile, 5-(1,2-Dihydro-2-thioxospiro[4H-3,1-benzoxazine-4,1-cyclohexan]-6-yl)-2-thiophenecarbonitrile, 6-(3-Chloro-4-fluorophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-4-propylthiophene-2-carbonitrile, 4-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-2-furonitrile, 4-Butyl-5-(4,4-dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)thiophene-2-carbonitrile, 6-(3-Bromophenyl)-4,4-dimethyl-1,4-dihydro-2H-3,1-benzoxazine-2-thione, and 2-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)thiophene-3-carbonitrile, or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

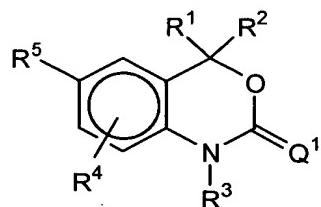
26(Original). The method according to claim 1, wherein said compound of formula I is 5-(4,4-Dimethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

27(Original). The method according to claim 1, wherein said compound of formula II is selected from the group consisting of: 5-(4-ethyl-4-methyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 5-(4,4-diethyl-2-thioxo-1,4-dihydro-2H-3,1-benzoxazin-6-yl)-1-methyl-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclobutan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclohexan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-(2-thioxo-1,2-dihydrospiro[3,1-benzoxazine-4,1'-cyclopantan]-6-yl)-1H-pyrrole-2-carbonitrile, 1-methyl-5-[2-thioxo-4,4-

bis(trifluoromethyl)-1,4-dihydro-2H-3,1-benzoxazine-6-yl]-1H-pyrrole-2-carbonitrile, and prodrugs, metabolites, and pharmaceutically acceptable salts thereof.

28(Currently Amended). A pharmaceutical kit useful for inducing contraception, said kit comprising a compound of formula I or formula II and at least one selective estrogen receptor modulator,

wherein formula I is:



I

wherein:

R<sup>1</sup> and R<sup>2</sup> are independent substituents selected from the group consisting of H, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>2</sub> to C<sub>6</sub> alkenyl, C<sub>3</sub> to C<sub>8</sub> cycloalkyl, phenyl, and thiophene;

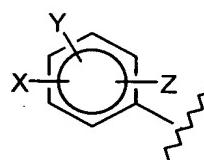
or R<sup>1</sup> and R<sup>2</sup> are fused to form a carbon-based 3 to 8 membered saturated spirocyclic ring;

R<sup>3</sup> is H;

R<sup>4</sup> is H;

R<sup>5</sup> is selected from the group consisting of (i) and (ii):

(i) a substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN, C<sub>1</sub> to C<sub>3</sub> alkyl, substituted C<sub>1</sub> to C<sub>3</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> alkoxy, NO<sub>2</sub>, and C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl;

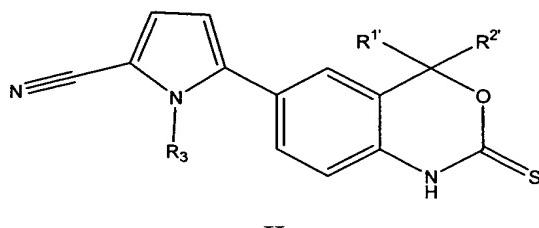
Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO<sub>2</sub>, C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>4</sub> alkyl, and substituted C<sub>1</sub> to C<sub>4</sub> alkyl; and

(ii) a five or six membered carbon-based heterocyclic ring having in its backbone 1 heteroatom selected from the group consisting of O, S, and NR<sup>6</sup> and having one or two independent substituents selected from the group consisting of H, halogen, CN, C<sub>1</sub> to C<sub>4</sub> alkyl, and substituted C<sub>1</sub> to C<sub>4</sub> alkyl;

R<sup>6</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, and C<sub>1</sub> to C<sub>4</sub> CO<sub>2</sub>alkyl;

Q<sup>1</sup> is S;

and formula II is:



wherein:

R<sup>1</sup> is selected from the group consisting of methyl, ethyl, and trifluoromethyl;

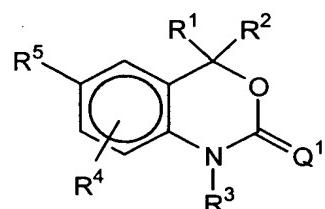
R<sup>2</sup> is selected from the group consisting of methyl, ethyl, and trifluoromethyl; or

R<sup>1</sup> and R<sup>2</sup> are joined to form a spirocyclic ring containing 3 to 7 carbon atoms; and R<sup>3</sup> is C<sub>1</sub> to C<sub>4</sub> alkyl; and

a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug thereof.

29(New). A contraceptive regimen comprising the periodic and discontinuous delivery of a compound of formula I or formula II, or a tautomer thereof, and a pharmaceutically effective amount of one or more of a selective estrogen receptor modulator to a female of child-bearing age,

wherein formula I is:



I

wherein:

$R^1$  and  $R^2$  are independent substituents selected from the group consisting of H, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>2</sub> to C<sub>6</sub> alkenyl, substituted C<sub>2</sub> to C<sub>6</sub> alkenyl, C<sub>2</sub> to C<sub>6</sub> alkynyl, substituted C<sub>2</sub> to C<sub>6</sub> alkynyl, C<sub>3</sub> to C<sub>8</sub> cycloalkyl, substituted C<sub>3</sub> to C<sub>8</sub> cycloalkyl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR<sup>A</sup>, and NR<sup>B</sup>COR<sup>A</sup>;

or  $R^1$  and  $R^2$  are fused to form a ring selected from the group consisting of a), b) and c), wherein said ring is optionally substituted by from 1 to 3 substituents selected from the group consisting of H and C<sub>1</sub> to C<sub>3</sub> alkyl;

- a) a carbon-based 3 to 8 membered saturated spirocyclic ring;
- b) a carbon-based 3 to 8 membered spirocyclic ring having one or more carbon-carbon double bonds; and
- c) a 3 to 8 membered spirocyclic ring having in its backbone one to three heteroatoms selected from the group consisting of O, S and N;

$R^A$  is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, substituted C<sub>1</sub> to C<sub>3</sub> alkyl, aryl, substituted aryl, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, amino, C<sub>1</sub> to C<sub>3</sub> aminoalkyl, and substituted C<sub>1</sub> to C<sub>3</sub> aminoalkyl;

$R^B$  is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

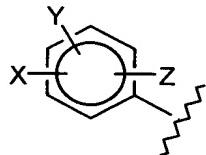
$R^3$  is selected from the group consisting of H, OH, NH<sub>2</sub>, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>3</sub> to C<sub>6</sub> alkenyl, substituted C<sub>3</sub> to C<sub>6</sub> alkenyl, alkynyl, substituted alkynyl, and COR<sup>C</sup>;

$R^C$  is selected from the group consisting of H, C<sub>1</sub> to C<sub>4</sub> alkyl, substituted C<sub>1</sub> to C<sub>4</sub> alkyl, aryl, substituted aryl, C<sub>1</sub> to C<sub>4</sub> alkoxy, substituted C<sub>1</sub> to C<sub>4</sub> alkoxy, C<sub>1</sub> to C<sub>4</sub> aminoalkyl, and substituted C<sub>1</sub> to C<sub>4</sub> aminoalkyl;

$R^4$  is selected from the group consisting of H, halogen, CN, NO<sub>2</sub>, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>1</sub> to C<sub>6</sub> alkoxy, substituted C<sub>1</sub> to C<sub>6</sub> alkoxy, C<sub>1</sub> to C<sub>6</sub> aminoalkyl, and substituted C<sub>1</sub> to C<sub>6</sub> aminoalkyl;

$R^5$  is selected from the group consisting of (i) and (ii):

- (i) a substituted benzene ring having the structure:



X is selected from the group consisting of halogen, CN, C<sub>1</sub> to C<sub>3</sub> alkyl, substituted C<sub>1</sub> to C<sub>3</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>3</sub> thioalkyl, substituted C<sub>1</sub> to C<sub>3</sub> thioalkyl, C<sub>1</sub> to C<sub>3</sub> aminoalkyl, substituted C<sub>1</sub> to C<sub>3</sub> aminoalkyl, NO<sub>2</sub>, C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl, substituted C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, COR<sup>D</sup>, OCOR<sup>D</sup>, and NR<sup>E</sup>COR<sup>D</sup>;

R<sup>D</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, substituted C<sub>1</sub> to C<sub>3</sub> alkyl, aryl, substituted aryl, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>3</sub> aminoalkyl, and substituted C<sub>1</sub> to C<sub>3</sub> aminoalkyl;

R<sup>E</sup> is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

Y and Z are independent substituents selected from the group consisting of H, halogen, CN, NO<sub>2</sub>, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>4</sub> alkyl, substituted C<sub>1</sub> to C<sub>4</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> thioalkyl, and substituted C<sub>1</sub> to C<sub>3</sub> thioalkyl; and

(ii) a five or six membered carbon-based heterocyclic ring having in its backbone 1, 2, or 3 heteroatoms selected from the group consisting of O, S, SO, SO<sub>2</sub>, and NR<sup>6</sup> and having one or two independent substituents selected from the group consisting of H, halogen, CN, NO<sub>2</sub>, C<sub>1</sub> to C<sub>4</sub> alkyl, substituted C<sub>1</sub> to C<sub>4</sub> alkyl, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>3</sub> aminoalkyl, substituted C<sub>1</sub> to C<sub>3</sub> aminoalkyl, C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl, substituted C<sub>1</sub> to C<sub>3</sub> perfluoroalkyl, 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted 5 or 6 membered carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, C<sub>1</sub> to C<sub>3</sub> thioalkyl, substituted C<sub>1</sub> to C<sub>3</sub> thioalkyl, COR<sup>F</sup>, and NR<sup>G</sup>COR<sup>F</sup>;

$R^F$  is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, substituted C<sub>1</sub> to C<sub>3</sub> alkyl, aryl, substituted aryl, C<sub>1</sub> to C<sub>3</sub> alkoxy, substituted C<sub>1</sub> to C<sub>3</sub> alkoxy, C<sub>1</sub> to C<sub>3</sub> aminoalkyl, and substituted C<sub>1</sub> to C<sub>3</sub> aminoalkyl;

$R^G$  is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

$R^6$  is selected from the group consisting of H, C<sub>1</sub> to C<sub>3</sub> alkyl, and C<sub>1</sub> to C<sub>4</sub> CO<sub>2</sub>alkyl;

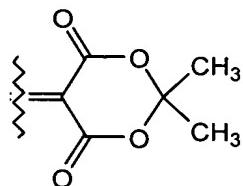
$Q^1$  is selected from the group consisting of S, NR<sup>7</sup>, and CR<sup>8</sup>R<sup>9</sup>;

$R^7$  is selected from the group consisting of CN, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>3</sub> to C<sub>8</sub> cycloalkyl, substituted C<sub>3</sub> to C<sub>8</sub> cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, SO<sub>2</sub>CF<sub>3</sub>, OR<sup>11</sup>, and NR<sup>11</sup>R<sup>12</sup>;

$R^8$  and  $R^9$  are independent substituents selected from the group consisting of H, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, C<sub>3</sub> to C<sub>8</sub> cycloalkyl, substituted C<sub>3</sub> to C<sub>8</sub> cycloalkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, NO<sub>2</sub>, CN, and CO<sub>2</sub>R<sup>10</sup>;

$R^{10}$  is selected from the group consisting of C<sub>1</sub> to C<sub>3</sub> alkyl and substituted C<sub>1</sub> to C<sub>3</sub> alkyl;

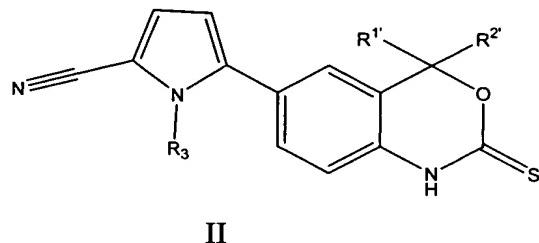
or CR<sup>8</sup>R<sup>9</sup> comprise a six membered ring having the structure:



$R^{11}$  and  $R^{12}$  are independently selected from the group consisting of H, C<sub>1</sub> to C<sub>6</sub> alkyl, substituted C<sub>1</sub> to C<sub>6</sub> alkyl, aryl, substituted aryl, carbon-based heterocyclic ring having in its backbone 1 to 3 heteroatoms, substituted carbon-based heterocyclic ring

having in its backbone 1 to 3 heteroatoms, acyl, substituted acyl, sulfonyl, and substituted sulfonyl;

and formula II is:



wherein:

$R^{1'}$  is selected from the group consisting of methyl, ethyl, and trifluoromethyl;

$R^{2'}$  is selected from the group consisting of methyl, ethyl, and trifluoromethyl; or

$R^{1'}$  and  $R^{2'}$  are joined to form a spirocyclic ring containing 3 to 7 carbon atoms; and  $R^{3'}$  is selected from the group consisting of  $C_1$  to  $C_4$  alkyl;

or a pharmaceutically acceptable salt, tautomer, metabolite, or prodrug of formula I or formula II.

30(New). The regimen according to claim 29, comprising delivering said compound of formula I or formula II and said selective estrogen receptor modulator separately.

31(New). The regimen according to claim 29, comprising delivering said compound of formula I or formula II and said selective estrogen receptor modulator in a single composition.

32(New). The regimen according to claim 29, further comprising delivering a placebo.

33(New). The regimen according to claim 29 which comprises 28 days.

34(New). The regimen according to claim 33, wherein said regimen comprises delivering said compound of formula I or formula II and said selective estrogen receptor modulator for 14 to 24 days.

35(New). The regimen according to claim 33, wherein said regimen comprises:

- (a) delivering said compound of formula I or formula II and said selective estrogen receptor modulator for 14 to 24 days; and
- (b) delivering said selective estrogen receptor modulator for 1 to 11 days.

36(New). The regimen according to claim 35, wherein said regimen further comprises:

- (c) delivering a placebo for 1 to 10 days.

37(New). The regimen according to claim 33, wherein said regimen comprises:

- (a) delivering said compound of formula I or formula II for 18 to 21 days; and
- (b) delivering said selective estrogen receptor modulator for 1 to 7 days.

38(New). The regimen according to claim 33, wherein said regimen comprises:

- (a) delivering said compound of formula I or formula II and an estrogen for 21 days; and
- (b) delivering said selective estrogen receptor modulator for 1 to 4 days.

39(New). The method according to claim 29, wherein said regimen comprises 28 days and the steps of:

- (a) a first phase of the compound of formula I or formula II and said selective estrogen receptor modulator to be administered on days 14 to 24 of said regimen;

- (b) a second phase of said selective estrogen receptor modulator to be administered on days 1 to 11 of said regimen; and
- (c) a third phase of an orally and pharmaceutically acceptable placebo for days 1 to 10 of said regimen or a third phase in which component (a) or (b) is not administered for days 1 to 10 of said regimen.

40(New). The method according to claim 39, wherein:

- (a) said first phase comprises 14 days;
- (b) said second phase comprises 7 days; and
- (c) said third phase comprises 7 days.